Prevalence of frailty using six screening and assessment tools amongst patients with chronic heart failure.

Short Title: Frailty identification in heart failure

Shirley Sze, MBBS[1]; Pierpaolo Pellicori, MD, FESC[1,2]; Jufen Zhang PhD[1,3]; Joan Weston[1]; Andrew L Clark, MA, MD, FRCP.[1]

[1]Department of Cardiology, Castle Hill Hospital, Hull York Medical School (at University of Hull), Kingston upon Hull, HU16 5JQ, UK

[2] Robertson Centre for Biostatistics & Clinical Trials, University of Glasgow & National Heart & Lung Institute, Imperial College, London, UK

[3] Faculty of Medical Science, Anglia Ruskin University, CB1 1PT, UK

Corresponding author: Shirley Sze

Department of Cardiology,

Hull York Medical School

Hull and East Yorkshire Medical Research and Teaching Centre

Castle Hill Hospital, Cottingham, Kingston upon Hull, HU16 5JQ, UK

Tel: + 44 1482 461811

Fax: +44 1482 461779

Email: Shirley.sze@nhs.net

Total word count: 4736 (including the title page, abstract, text, references, tables, and figures legends)

Dr. Sze – Screening 11.8.2018

Abstract:

Background:

Frailty is common in patients with chronic heart failure (CHF) and is associated with adverse outcome, but few data exist.

Objectives:

To report the prevalence of frailty and agreement amongst 3 frailty assessment tools and 3 screening tools in CHF patients.

Methods:

We used the following frailty screening tools: the clinical frailty scale (CFS); the Derby frailty index (DFI); and the acute frailty network (AFN) frailty criteria. We used the following frailty assessment tools: the Fried criteria; the Edmonton frailty score (EFS); and the deficit index (DI).

Results:

467 consecutive ambulatory CHF patients (67% male, median age 76 (interquartile range (IQR):69-82 years), median NTproBNP 1156 (IQR:469-2463) ng/L) and 87 controls (79% male, median age 73 (IQR:69-77 years) were studied. The prevalence of frailty using the different tools was higher in CHF patients than in controls (30-52% vs 2-15%, respectively).

Frail patients tended to be older, have worse symptoms, higher NTproBNP and more co-morbidities. Of the screening tools, CFS had the strongest correlation and agreement with the assessment tools (correlation coefficient: 0.86-0.89, kappa coefficient: 0.65-0.72, depending on the frailty assessment tools, all $p<0.001$). CFS had the highest sensitivity (87%) and specificity (89%) amongst screening tools and the lowest misclassification rate (12%) amongst all 6 frailty tools in identifying frailty according to the standard combined frailty index.

Conclusion:

Frailty is common in CHF patients and is associated with increasing age, co-morbidities and severity of HF. CFS is a simple screening tool which identifies a similar group as more lengthy assessment tools.

(250 words)

Key words: heart failure, frailty screening, assessment

Abbreviations: CHF = chronic heart failure, LVEF = left ventricular ejection fraction, NTproBNP = N-terminal pro B-type natriuretic peptide, HeFREF = heart failure with reduced ejection fraction, HeFNEF = heart failure with normal ejection fraction, DFI = Derby frailty index, AFN = the acute frailty network criteria, CFS = clinical frailty scale, EFS = Edmonton frailty scale, DI = the deficit index

Dr. Sze – Screening 11.8.2018

Introduction:

Frailty is common in patients with chronic heart failure (CHF) and is associated with increased risk of death and hospitalisations.[1,2,3] However, there is no standard method for evaluating frailty in patients with CHF.

Tools to evaluate frailty stem from two basic concepts of frailty – physical frailty and multi-dimensional frailty.

- The first was proposed by Fried and colleagues, who defined frailty as a physical syndrome using five criteria (Fried criteria): weak grip strength, unintentional weight loss, exhaustion, slow walking speed and low physical activity.[4]
- The second concept was proposed by Rockwood et al who defined frailty as a state of vulnerability due to accumulation of health deficits. Frailty is measured by a deficit index which quantifies the cumulative burden of deficits. [5,6] The Edmonton frailty scale (EFS) is a simplified frailty assessment tool based on the concept of multi-dimensional frailty which has been shown to have good construct validity and reliability.[7]

Despite their prognostic value and wide-spread use in research, the Fried criteria and the deficit index are not routinely used in clinical practice as they are time consuming to perform. Simple screening tools[8 9 10] have been developed, but it is not clear whether they identify the same patients as the more comprehensive assessment tools.

Very few studies have simultaneously evaluated different tools to quantify frailty in the same cohort of patients with CHF.[11] To the best of our knowledge, no study has ever compared the efficacy of frailty screening tools versus assessment tools in patients with CHF. We therefore evaluated frailty in a cohort of patients with CHF using 3 commonly used frailty screening tools and 3 commonly used frailty assessment tools. We compared the efficacy of simple screening tools versus more comprehensive assessment tools in detecting frailty in patients with CHF.

Methods

Study population

Consecutive ambulatory patients with CHF attending a community heart failure clinic were enrolled between September 2016 and March 2017. All patients had a pre-existing (>1 year) clinical diagnosis of CHF confirmed by either evidence of left ventricular systolic dysfunction on echocardiography (left ventricular ejection fraction (LVEF) <40% or at least moderate left ventricular systolic dysfunction by visual inspection if LVEF was not calculated), defined as heart failure with reduced ejection fraction, HeFREF; **or** normal left ventricular systolic function (LVEF ≥40% or better than, or equal to, mild-moderate left ventricular systolic dysfunction by visual inspection) and N-terminal pro-B-type natriuretic peptide (NTproBNP) >400 ng/L, defined as heart failure with normal ejection fraction, HeFNEF.[12]

All patients had already been initiated on guideline-indicated treatment for heart failure and were regularly followed up.

Subjects who had previously consented to take part in research were recruited as controls. Control subjects were older than 65 years of age, with no previous or current symptoms or signs of HF and with normal left ventricular systolic function on echocardiography who also had risk factors for development of HF, including coronary artery disease, diabetes mellitus or hypertension.

During the visit, all patients had a full medical history, physical examination, blood tests (full blood count, urea and electrolytes and NTproBNP), an electrocardiogram and a consultation with a HF specialist.

Frailty screening and assessment

All patients and controls were screened and assessed by the same researcher (SS) for frailty (Appendix 1a)

The screening tools used were:

1) *The Derby frailty index* (DFI; scores as frail vs non-frail)

   DFI is a quick pragmatic frailty identification tool initially developed in 2013.[9] A patient is classified as frail if one of the following criteria is met: 1) ≥65 years old and a care home resident; 2) ≥75 years old with confusion, falls or reduced mobility; 3) ≥ 85 years old with >4 co-morbidities.

2) *The acute frailty network criteria* (AFN; scores as frail vs non-frail)

AFN defines frailty as present in (a) people aged ≥85 years or (b) people aged ≥65 years with one or more of the following presenting features: cognitive impairment; resident in a care home; history of fragility fractures; Parkinson's disease; recurrent falls.[10]

3) *The clinical frailty scale* (CFS; measures between 1 (very fit) and 9 (terminally ill))

Subjects are scored according to their functional capacity, level of dependence and co-morbidities. For example, a patient with uncontrolled symptoms who is not frankly dependent is classified as vulnerable and scores 4 on the CFS; while an individual with limited dependence on others for instrumental activities of daily living including finances, transportation, heavy housework and medications will be classified as mildly frail and scores 5 on the CFS. Subjects with a CFS >4 are classified as frail.[8]

The assessment tools used were:

1) *Fried frailty phenotype* (measures between 0 (normal) and 5 (very frail)):

The Fried Frailty phenotype[4] is commonly used to validate other frailty criteria. Frailty is considered as a clinical syndrome based on five criteria: unintentional weight loss (≥10 lbs [≥4.5 kg] in the past year); self-reported exhaustion; weakness (low grip strength); slow walking speed (time to walk 5 meters ≥ 6-7 seconds depending on sex and height); and low physical activity (low weekly total energy expenditure assessed using the short version of the Minnesota Leisure Time Activity

questionnaire[13].) (Appendix 1b) Subjects with ≥ 3 points are classified as frail and those with 1-2 points and 0 points are classified as pre-frail and non-frail respectively.

2) *Edmonton frailty scale* (EFS; measures between 0-17)

EFS is a multi-dimensional frailty assessment tool which includes general health status, functional independence, social support, cognition, medication use, nutrition, continence and mood.[7] EFS has been validated against the comprehensive geriatric assessment (CGA),[14] a multi-dimensional, multidisciplinary diagnostic process used to determine medical, functional and psychosocial problems in elderly patients.[7] Subjects with EFS 0-5 are classified as non-frail, those with EFS 6-7, 8-9, 10-11 and 12-17 are classified as vulnerable, mildly, moderately and severely frail respectively. Subjects with EFS ≥ 8 are classified as frail. (Appendix 1c)

3) The Deficit Index (DI; measures between 0.03-0.72)

Mitnitski and Rockwood consider frailty as a clinical state as a result of accumulation of deficits (symptoms, signs, co-morbidities and disabilities).[15] These deficits are combined in a frailty index score to reflect the proportion of potential deficits present in a person. We selected 32 deficits according to previously published criteria[6] to construct the deficit index. The first 14 items of the DI were related to activities of daily living which were collected by direct questioning of participants. The remaining items were based on information from patient's medical records or physical tests during the visit. If a subject exhibited 5 out of the 32 possible deficits, the frailty index for that patient would be 5/32 or 0.16. We stratified patients and controls

according to terciles of DI; those in the lower tercile were classified as non-frail while those in the middle and upper terciles were classified as pre-frail and frail respectively. (Appendix 1d)

Physical Tests:

a) Handgrip strength (HGS):

Hand grip strength was obtained with a handgrip dynamometer (Es-100 Ekj107, Evernew, Japan). The subject was seated with forearm resting on the arm of a chair and instructed to hold the dynamometer upright and squeeze as hard as possible. Three trials in the right hand followed by three trials in the left hand were recorded and the highest reading of the 6 was taken as the final reading.

b) Gait analysis

1) Timed get up and go test:

The area for the timed get up and go test was set up by measuring 3 meters from the front legs of a straight-backed armchair. The subject was instructed to: "Sit with your back against the chair and your arms on the arm rests. On the word `go,' stand upright, then walk at your normal pace to the line on the floor, turn around, return to the chair, and sit down." The time required to complete the test was time from the word `go' to time when the subject returned to the starting position. Subjects who took more than 10 seconds to complete the test were classified as frail. (Appendix 1c)

2) Five metre walk test:

The subject was instructed to walk at a normal pace for 5 meters according to their ability. The time required to complete the test was time from the word `go' to time when the subject reached the 5-meter-point. Subjects who took more than 6-7 seconds (depending on sex and height) to complete the test were classified as frail. (Appendix 1b)

Co-morbidities

Co-morbidities were measured using the Charlson co-morbidity index/score.[16] Hypertension was defined as systolic blood pressure ≥140 mmHg, diastolic blood pressure ≥90 mmHg or a previous clinical diagnosis.[17] Current haemoglobin (Hb) levels were used to define anaemia (Hb <13.0 g/dL in men and <12.0 g/dL in women).[18] Diabetes mellitus was defined according to the guideline from Diabetes UK.[19] Patients consented to the use of electronic medical records to identify previous clinical history of myocardial infarction, peripheral vascular disease, cerebrovascular disease, chronic obstructive pulmonary disease (COPD), dementia, rheumatological disease, peptic ulcer, hemiplegia/ paraplegia, liver or renal disease or malignancy.

Statistical analysis

Continuous data are expressed as a median with interquartile range (IQR) (25^{th} to 75^{th} centiles) and categorical data are expressed as n (%). Independent t tests and Mann-Whitney U tests were used to compare two continuous variables for normally and non-normally distributed data. The chi-squared test was used to compare proportions between groups. Pearson's correlation or Spearman's correlation coefficients were used to assess the

relationships between two variables. Venn diagrams were used to illustrate the relationship between screening and assessment tools. Kappa statistics were used to study the agreement between frailty screening tools and assessment tools.

Since there is no gold standard in evaluating frailty in patients with CHF, for each of the frailty tools, we used the results of the *other* 5 tools to produce a single combined frailty index which we assumed to be the gold standard frailty tool. This methodology has been previously suggested by Pablo et al.[20] Similarly, for each of the physical tests (timed get up and go test, 5 metre walk test and hand grip strength), we used the results of the 5 frailty tools which do not include the physical test, to produce a single combined frailty index as the gold standard frailty tool. Subjects were defined as frail if so identified by at least 3 of the 5 tools. The sensitivity, specificity and predictive values for each of the individual tools and physical tests in identifying frailty according to the combined index were calculated.

To investigate the bias associated with CFS being a subjective frailty screening tool, in addition to the principal investigator (SS), a second investigator (JW) also completed the CFS for a random sample of 23 patients. Kappa statistics were used to determine the inter-operator agreement.

All statistical analyses were performed using SPSS 22 (SPSS INc.,Chicago, IL, USA) and The Stata (14th Version, StataCorp, TX, USA) statistical computer package. A two-tailed P-value of <0.05 was considered significant in all analyses.

The study conformed to the principles outlined in the Declaration of Helsinki and was approved by relevant ethical bodies. All subjects gave their written informed consent for their data to be used for research.

Results

A total of 467 consecutive patients with CHF and 87 controls was studied. Table 1a shows the baseline characteristics of the HF cohort vs controls. The majority of patients and controls were male and elderly; 17% of those with CHF were older than 85 years (vs 2% of controls). Most of the patients with CHF had HeFREF (62%) with a median NTproBNP of over 1100ng/L; around one fifth had severe symptoms (NYHA III/IV).

Prevalence of frailty

The prevalence of frailty varied according to frailty tools used. It was much more common in patients than in controls, regardless of the frailty tool used (HF: 30-52% vs controls: 2-15%). (Table 2)

Amongst the frailty assessment tools, the Fried criteria scored the greatest proportion of patients as frail (52%) while EFS scored the lowest proportion as frail (30%) (Figure 1). 26% (N=119) of patients were classified as frail by **all** 3 assessment tools. (Central illustration)

Amongst the frailty screening tools, DFI scored the greatest proportion of patients as frail (48%) while CFS scored the lowest proportion as frail (44%) (Figure 1). 27% (N=128) of patients were classified as frail by **all** 3 screening tools. (Central illustration)

The prevalence of frailty was higher in patients with HeFNEF than HeFREF. (Table 3) The prevalence of frailty was higher in patients with atrial fibrillation (AF) than in those in sinus rhythm. The prevalence of frailty increased with decreasing BMI and increasing NYHA class, age and NTproBNP.

Prevalence of pre-frailty

The prevalence of pre-frailty varied greatly depending on the assessment tool used. (Table 2) According to the EFS, the prevalence of pre-frailty was much higher in patients than controls, but according to the Fried criteria, pre-frailty was as common in both groups.

The Fried criteria scored the greatest proportion of patients as pre-frail (32%) while the EFS scored the lowest proportion as pre-frail (19%). (Figure 1) Only 3% (N=13) of patients were classified as 'pre-frail' by **all** 3 assessment tools (Appendix 2)

Relationship between frailty and clinical data

Compared to those who are not frail, frail patients were older, had worse symptoms, higher NTproBNP, worse renal function and anaemia. They were more likely to be on diuretics but less likely to be on ACE-inhibitors, beta-blockers and mineralocorticoid antagonist; they also

had a lower BMI and more co-morbidities: especially dementia, COPD, depression, recurrent falls and incontinence. (Table 1b)

Relationship between different frailty tools

The relationship between the results of the frailty scores is shown in Table 4. Of the 3 frailty *screening* tools, CFS had the strongest correlation with the frailty *assessment* tools (correlation coefficient: 0.86-0.89, depending on the frailty assessment tools, all $P<0.001$)

Detection of frailty: screening tools vs assessment tools

Of the screening tools, CFS had the highest and DFI the lowest agreement with the assessment tools in distinguishing between frail and non-frail patients. (Table 5)

Frailty tools *vs* combined index

Table 6 shows the sensitivity, specificity and misclassification rates of different frailty tools (screening vs assessment vs single physical tests) in identifying frailty according to the combined index (the presumed gold standard for identifying frailty).

Of the screening tools, CFS had the highest sensitivity (87%) and specificity (89%). DFI had the highest false positive rate (16%) and false negative rate (10%). CFS had the lowest misclassification rate (12%).

Of the assessment tools, the Fried criteria had the highest sensitivity (93%) and EFS had the highest specificity (98%). The Fried criteria had the highest false positive rate (14%) and EFS has the highest false negative rate (18%).

Of the three single physical tests, timed get up and go test had the highest sensitivity (97%) and 5m walk test had the highest specificity (59%). Grip strength had the highest false positive rate (25%) and false negative rate (3%). Overall, timed get up and go test had the lowest misclassification rate (25%).

Compared to frailty assessments or screening tools, single physical tests have higher overall sensitivities but lower specificities and higher misclassification rates.

Inter-operator agreement of CFS:

There was close agreement between the two operators' judgements on degree of frailty in a random sample of subjects (N=23) using the CFS, with a Kappa coefficient (K) of 0.72 (95% CI: 0.51-0.93, $p<0.001$).

Time needed to complete frailty screening vs assessment:

Frailty screening on average takes no more than 1 minute to complete, whereas frailty assessment on average takes 15 minutes to complete, depending on the mobility of patients.

Discussion

We found that frailty is very common amongst outpatients with CHF, but that the prevalence varied from 30 to 52% depending on the assessment tool used. Our findings are similar to those from a meta-analysis involving 5522 ambulatory patients with CHF or older adults aged 70 to 79 years. Frailty was assessed by several tools including the Fried criteria, comprehensive geriatric assessment, the deficit index, frailty staging system, modified frailty scale and the Health ABC Short Physical Performance Battery (HABC battery) and Gill index. The prevalence of frailty was between 18 and 54% depending on the population studied.[21] There was substantial variance in prevalence of frailty in the meta-analysis probably due to heterogeneity of populations studied. Our results are a more accurate reflection of the true prevalence of frailty in patients with CHF as we evaluated frailty using 6 different scoring tools in the same cohort of patients.

Frailty was more common in patients with HeFNEF than in patients with HeFREF. The patients with HeFNEF were older and had a greater burden of non-cardiac co-morbidities, themselves associated with reduced functional status and increased risk of hospitalisation.[22,23] AF becomes more common with age, and is particularly common in patients with HeFNEF. It is itself associated with the development and progression of frailty.[24]

Ours is the first paper to compare simple frailty screening tools with more comprehensive assessment tools in patients with CHF. Whilst we found that there was substantial overlap between patients identified as frail by each tool, the overlap was not very great. Although we found a correlation between frailty screening and assessment tools, the relation was modest

for some, suggesting that the tools are measuring differing aspects of a common phenotype, and that none is on its own definitive.

The different tools have strengths and weaknesses. The Fried criteria objectively measure physical functioning, but other domains, particularly cognition, are not considered. The DI covers multiple domains including physical functioning and co-morbidities, and is thus a more comprehensive tool than the Fried criteria. The EFS, similar to DI, also examines multiple domains including cognition, social support, medication, nutrition and mood; it also includes straightforward physical performance measures (timed get up and go test). Frailty assessments require significant time to perform (on average 10-15 minutes depending on the mobility of patients), which is not ideal in busy clinical settings.

Screening tools are much easier to use. They do not require physical measurements to be carried out and can be completed within a minute. Amongst the screening tools, CFS has the highest sensitivity and specificity with the lowest misclassification rate. We found that CFS, was as effective as lengthy frailty assessments in detecting frailty, and it is therefore appealing for use in clinical practice. CFS has a subjective component, but we found inter-operator agreement to be good.

Worsening results on physical performance measures such as grip strength and walking speed predict increasing mortality and risk of institutionalisation.[25,26] We found that single physical tests have higher sensitivities but lower specificities than frailty assessment or screening tools, and higher misclassification rates. Further studies will clarify whether single physical

measures or simple frailty screening tools have comparable prognostic value to more comprehensive frailty assessments.

Study limitations

Firstly, because this is a single-centre study conducted in the UK with limited sample size, external validation of our results from other populations with different healthcare and social systems is needed. Our study is, however, the largest study which directly compares several commonly used frailty screening and assessment tools in consecutive, unselected, patients with CHF.

Secondly, we have only studied 6 of the most commonly used frailty tools in literature. A large number of frailty screening and assessment tools has been proposed and identified patients at risk of adverse outcome in other clinical scenarios.[27]

Thirdly, this study only focuses on reporting prevalence of frailty by the different tools, but we have not evaluated the predictive role of these tools.

Fourthly, we only included patients with a diagnosis of dementia if they had capacity in the investigator's opinion to consent for the study. We are therefore unable to report on frailty in patients with dementia so severe as to be considered lacking in capacity.

Conclusion

Frailty is common in patients with CHF. CFS is a short and easy to use frailty screening tool, which has comparable effectiveness to lengthy frailty assessments in identifying frailty. CFS should therefore be considered when assessing patients with CHF to enable identification of at-risk individuals. Further work is required to study the prognostic value of simple screening vs assessment tools in patients with CHF.

Perspectives:

Competency in medical knowledge 1: Frailty is common in patients with CHF, with a prevalence of 30 -52% depending on the screening or assessment tool used.

Competency in medical knowledge 2: Frailty is associated with increasing age, co-morbidities and severity of HF.

Competency in medical knowledge 3: CFS is a short and easy to use frailty screening tool which has comparable effectiveness to lengthy frailty assessments in identifying frailty in patients with CHF. CFS should be considered when assessing patients with CHF.

Translational outlook: Recognition of the high prevalence of frailty in patients with CHF should stimulate further research on the prognostic value of simple screening vs assessment tools.

Acknowledgement: None

Funding: None

Conflict of interest: None

Legends

Tables

Table 1a. Baseline characteristics of HF cohort vs controls

Table 1b. Baseline characteristics of frail vs non-frail HF patients categorised according to different frailty assessment tools.

Table 2. Prevalence of pre-frailty and frailty in HF vs controls according to different frailty tools.

Table 3. Prevalence of frailty in different subgroups of patients with CHF.

Table 4: Correlation coefficients for frailty tools.

Table 5. Agreement between frailty screening vs assessment tools.

Table 6. Sensitivity, specificity and misclassification rates of different frailty tools (screening vs assessment vs single physical tests) in identifying frailty according to the combined index (the presumed gold standard for identifying frailty).

Figures

Figure 1 Bar graph showing prevalence of frailty and pre-frailty by different frailty tools in the HF cohort.

Central illustration: Venn diagrams showing the relationship between different assessment and screening tools in detecting frailty in patients with HF and in controls.

Appendix

Appendix 1a. Evaluation of frailty by frailty screening tools.

Appendix 1b. Evaluation of frailty by Fried criteria

Appendix 1c. Evaluation of frailty by Edmonton frailty scale

Appendix 1d. Evaluation of frailty by Deficit index

Appendix 2: Venn diagrams showing the relationship between different tools in detecting pre-frailty in patients with HF and in controls.

REFERENCES

[1] Denfeld QE, Winters-Stone K, Mudd J O, Gelow J M, Kurdi S, Lee C S. The prevalence of frailty in heart failure: A systematic review and meta-analysis, *Int J Cardiol* 2017; **236**: 283-289.

[2] Cacciatore F, Abete P, Mazzella F, et al. Frailty predicts long-term mortality in elderly subjects with chronic heart failure. Eur J Clin Invest. 2005;**35**:723–30.

[3] Chaudhry SI, Wang Y, Gill TM, et al. Geriatric conditions and subsequent mortality in older patients with heart failure. J Am Coll Cardiol. **55**:309–16.

[4] Fried LP, Tangen CM, Walston J, et al. Frailty in older adults: evidence for a phenotype. J Gerontol A Biol Sci Med Sci. 2001;**56**:M146–56.

[5] Rockwood K, Andrew M, Mitnitski A. A comparison of two approaches to measuring frailty in elderly people. J Gerontol A Biol Sci Med Sci. 2007;**62**:738–43.

[6] Searle SD, Mitnitski A, Gahbauer EA, et al. A standard procedure for creating a frailty index. BMC Geriatrics. 2008;**8**:24.

[7] Rolfson DB, Majumdar SR, Tsuyuki RT, Tahir A, Rockwood K. Validity and reliability of the Edmonton Frail Scale. *Age and Ageing.* 2006;**35**:526-529.

[8] Rockwood K, Song X, MacKnight C, et al. A global clinical measure of fitness and frailty in elderly people. *CMAJ* 2005;**173**:489–495.

[9] Woodard J, Youde J, Sutton B & Bagshaw S. Frailty Identification in Acute Medical Admissions. *Age Ageing* 2014;**43**:i9.

[10] Acute frailty nework webpage. [Accessed June 2018]; available at: http://www.acutefrailtynetwork.org.uk/uploads/files/1/Resource/SILVER_BOOK_FINAL_MAIN.pdf

[11] McNallan SM, Chamberlain AM, Gerber Y, et al. Measuring Frailty in Heart Failure: A Community Perspective. *AHJ*. 2013;**166**:10.

[12] Ponikowski P, Voors AA, Anker SD et Authors/Task Force Members; Document Reviewers. 2016 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure: The Task Force for the diagnosis and treatment of acute and chronic heart failure of

the European Society of Cardiology (ESC). Developed with the special contribution of the Heart Failure Association (HFA) of the ESC. *Eur J Heart Fail*. 2016;**18**:891-975.

[13] Montoye HJ, Kemper HCG, Saris WHM, Washburn RA. Measuring physical activity and energy expenditure. Champaign: Human Kinetics, 1996.

[14] Rubenstein LZ, Stuck AE, Siu AL, Wieland D. Impacts of geriatric evaluation and management programs on defined outcomes: overview of evidence. *J Am Geriatr Soc*. 1991;**39**:8S-16S.

[15] Mitnitski AB, Graham JE, Mogilner AJ, Rockwood K. Frailty, fitness and late-life mortality in relation to chronological and biological age. BMC Geriatrics 2002, 27(2):1.

[16] Charlson ME, Pompei P, Ales KL, MacKenzie CR. A new method of classifying prognostic comorbidity in longitudinal studies: development and validation. *J Chronic Dis* 1987;**40**:373-383.

[17] Chobanian AV, Bakris GL, Black HR, et al. The Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure: the JNC 7 report. *JAMA.* 2003;**289**:2560–72.

[18] Janz TG, Johnson RL, Rubenstein SD. Anemia in the emergency department: evaluation and treatment. *Emergency Medicine Practice*.2013;1**5**:1-15.

[19] Diagnostic criteria for diabetes. Diabetes UK. URL: https://www.diabetes.org.uk/Professionals/Position-statements-reports/Diagnosis-ongoing-management-monitoring/New_diagnostic_criteria_for_diabetes/ (Last accessed on 27th June 2017)

[20] Pablo AR, Izaga MA, Alda LA. Assessment of nutritional status on hospital admission: nutritional scores. *Eur J Clin Nutr* 2003;**57**:824-831.

---

[21] Jha SR, Ha HS, Hickman LD et al. Frailty in advanced heart failure: a systematic review. *Heart Fail Rev*. 2015;**20**:553-60.

[22] Chan MM, Lam CS. How do patients with heart failure with preserved ejection fraction die? *Eur J Heart Fail*. 2013;**15**:604-13.

[23] Ather S, Chan W, Bozkurt B, et al. Impact of noncardiac comorbidities on morbidity and mortality in a predominantly male population with heart failure and preserved versus reduced ejection fraction. *J Am Coll Cardiol*. 2012;**59**:998-1005.

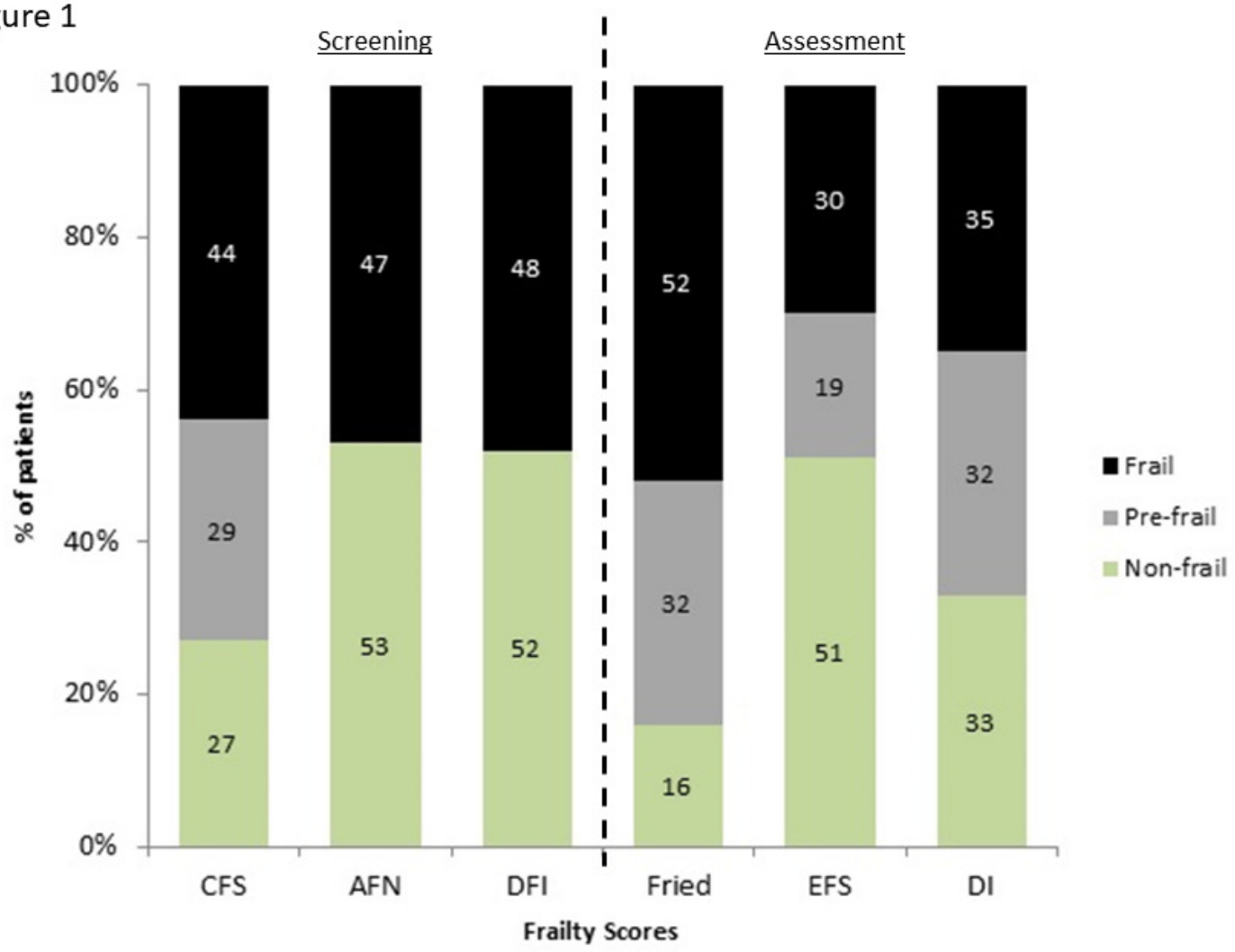
[24] Pardaens K, Van Cleemput J, Vanhaecke J, Fagard RH. Atrial fibrillation is associated with a lower exercise capacity in male chronic heart failure patients. Heart. 1997;78:564–568.

[25] Gale CR, Martyn CN, Cooper C. Grip strength, body composition, and mortality. *Int J Epidemiol* 2007;**36**:228–235.

[26] Woo J, Ho SC, Yu AL. Walking speed and stride length predicts 36 months dependency, mortality, and institutionalization in Chinese aged 70 and older. *J Am Geriatr Soc* 1999;**47**:1257–1260.

[27] Afilalo J, Lauck S, Kim DH, et al. Frailty in older adults undergoing aortic valve replacement: the FRAILTY- AVR Study. *J Am Coll Cardio*. 2017;**70**:689-700.

Figure 1


Screening
Assessment
100%
80%
60%
40%
20%
0%
% of patients
44
29
27
47
53
48
52
52
52
32
16
30
19
51
35
32
33
CFS
AFN
DFI
Fried
EFS
DI
Frailty Scores
Frail
Pre-frail
Non-frail

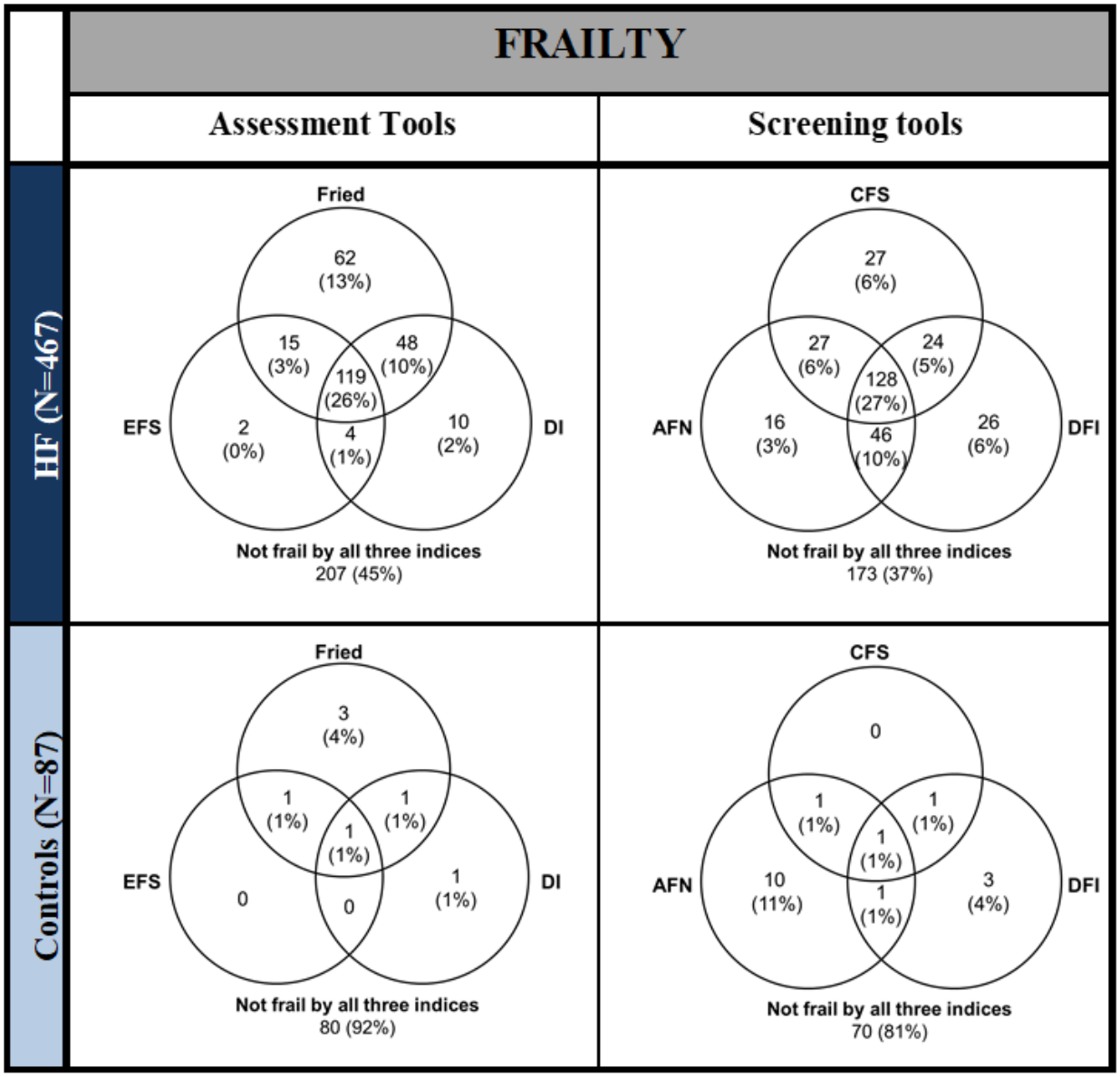

FRAILTY
Assessment Tools
Screening tools
HF (N=467)
Controls (N=87)
Fried
62 (13%)
15 (3%)
48 (10%)
119 (26%)
EFS
2 (0%)
4 (1%)
10 (2%)
DI
Not frail by all three indices
207 (45%)
CFS
27 (6%)
27 (6%)
24 (5%)
128 (27%)
AFN
16 (3%)
46 (10%)
26 (6%)
DFI
Not frail by all three indices
173 (37%)
Fried
3 (4%)
1 (1%)
1 (1%)
1 (1%)
EFS
0
0
1 (1%)
DI
Not frail by all three indices
80 (92%)
CFS
0
1 (1%)
1 (1%)
1 (1%)
AFN
10 (11%)
1 (1%)
3 (4%)
DFI
Not frail by all three indices
70 (81%)

Table 1a. Baseline characteristics of HF cohort vs controls.

	Controls (N=87)	HF (N=467)	p	Missing
Demographics				
Age, years	73 (69-77)	76 (69-82)	0.11	0
Age≥85 years, n(%)	2(2)	81(17)	<0.001	0
Sex (male), n(%)	69(79)	313(67)	0.02	0
HR (bpm)	61 (55-70)	70 (60-80)	<0.001	0
BP systolic (mmHg)	144 (130-152)	139 (126-162)	0.98	0
BP diastolic (mmHg)	76 (70-82)	75 (66-83)	0.40	0
NYHA, n(%) I/II III/IV	 - -	 364 (78) 103 (22)		0
HF phenotype, n(%) HeFREF HeFNEF	NA	 291 (62) 176 (38)		0
LVEF (%)	58 (53-64)	45 (35-54)	<0.001	160
LV systolic impairment, n(%) None-mild Moderate-severe	 87 (100) 0	 252 (54) 215 (46)	<0.001	0
Height (m)	1.71 (1.63-1.75)	1.68 (1.61-1.75)	0.20	0
Weight (kg)	81 (73-92)	83 (69-99)	0.22	0
BMI (kg/m^2)	27.8 (25.2-30.8)	29.0 (25.0-33.2)	0.08	0
BMI categories (kg/m^2) <24.9 25.0-29.9 ≥30.0	 18 (21) 42 (48) 27 (31)	 111 (24) 158 (34) 198 (42)	0.03	0
Comorbidities				
Charlson score	6 (4-7)	8 (6-10)	<0.001	0
MI, n(%)	27 (31)	198 (42)	0.05	0
PVD, n(%)	16 (18)	72 (15)	0.49	0
HTN, n(%)	61 (70)	313 (67)	0.57	0
CVA/TIA, n(%)	5 (6)	71 (15)	0.02	0
Diabetes, n (%)	35 (40)	163 (35)	0.24	0
Dementia, n(%)	1 (1)	48 (10)	0.006	0
COPD, n(%)	16 (18)	140 (30)	0.03	0
Depression, n(%)	9 (10)	93 (20)	0.03	0
Anaemia, n(%)	22 (25)	218 (47)	<0.001	0

Recurrent falls, n(%)	5 (6)	173 (37)	<0.001	0
Incontinence, n(%)	1 (1)	33 (7)	0.04	0
Medications				
BB, n(%)	57 (66)	392 (84)	<0.001	0
ACEi/ARB, n(%)	51 (59)	389 (83)	<0.001	0
MRA, n(%)	1 (1)	214 (46)	<0.001	0
Digoxin, n(%)	0	100 (21)	<0.001	0
Loop diuretic, n(%)	3 (3)	347 (74)	<0.001	0
Thiazide, n(%)	8 (9)	17 (4)	0.02	0
≥5 medications, n (%)	58 (67)	404 (87)	<0.001	0
Blood tests				
NTproBNP (ng/L)	170 (99-278)	1156 (496-2463)	<0.001	2
Hb (g/dL)	139 (127-147)	131 (118-142)	0.007	0
Na (mmol/L)	137 (136-139)	137 (135-138)	0.01	0
K (mmol/L)	4.4 (4.2-4.6)	4.4 (4.2-4.7)	0.11	0
eGFR (mL/min per 1.73 m^2)	77 (64-87)	55 (40-73)	<0.001	0
Frailty screening/ assessments				
Weekly energy expenditure (kcal x kg^{-1} x wk^{-1})	1080 (735-1593)	420 (105-853)	<0.001	0
5 m walk test (>6-7sec), n(%)	10 (12)	294 (63)	<0.001	0
TUGT >10sec, n(%)	19 (22)	325 (69)	<0.001	0
Grip strength (kg)	34 (22-40)	20 (14-33)	<0.001	0
<u>Frailty screening</u>				0
CFS (>4), n(%)	3 (3)	206 (44)	<0.001	
AFN (frail), n(%)	13 (15)	217 (47)	<0.001	
DFI (frail), n(%)	6 (7)	224 (48)	<0.001	
<u>Frailty assessment</u>				0
Fried criteria	0 (0-1)	3 (1-4)	<0.001	
Deficit index	0.14 (0.11-0.19)	0.28 (0.20-0.38)	<0.001	
Edmonton frailty scale	2 (1-3)	5 (3-8)	<0.001	

HF= heart failure, HR= heart rate, BP= blood pressure, NYHA= new York heart association, HeFREF= heart failure with reduced ejection fraction, HeFNEF= heart failure with normal ejection fraction, LVEF= left ventricular ejection fraction, BMI= body mass index, MI= myocardial infarction, PVD= peripheral vascular disease, HTN= hypertension, CVA/TIA= cerebrovascular accident/ transient ischaemic attack, COPD= chronic obstructive pulmonary disease, BB= beta-blocker, ACEi= angiotensin converting enzyme inhibitor, ARB= angiotensin receptor blocker, MRA= mineralocorticoid receptor antagonist, NTproBNP= N-terminal pro-B-type natriuretic peptide, Hb= haemoglobin, Na= sodium, K= potassium, eGFR = estimated glomerular filtration rate, 5m= 5 meter, TUGT= timed get up and go test, CFS= clinical frailty scale, AFN= acute frailty network frailty criteria, DFI= Derby frailty index.

Table 1b. Baseline characteristics of frail vs non-frail HF patients categorised according to different frailty assessment tools.

	Frailty Assessment in patients with HF (N=467)									Missing
	Fried criteria			Deficit Index			Edmonton Frail Scale			
	Non-frail (N=223)	Frail (N=244)	p	Non-frail (N=302)	Frail (N=165)	p	Non-frail (N=327)	Frail (N=140)	p	
Demographics										
Age, years	72 (64-78)	80 (74-84)	<0.001	74 (66-80)	80 (74-85)	<0.001	74 (66-80)	80 (75-85)	<0.001	0
Age≥85 years, n(%)	21(9)	60(25)	<0.001	38(13)	44(27)	<0.001	42(13)	39(28)	<0.001	0
Sex (male), n(%)	165(74)	148(61)	0.002	214(71)	99(60)	0.02	224(69)	89(64)	0.30	0
HR (bpm)	70 (61-77)	71 (60-82)	0.14	70 (60-80)	70 (62-82)	0.80	70 (60-79)	70 (61-83)	0.21	0
BP systolic (mmHg)	140 (125-157)	138 (126-166)	0.17	140 (125-158)	137 (128-167)	0.15	141 (126-162)	137 (125-162)	0.79	0
BP diastolic (mmHg)	74 (67-83)	75 (65-83)	0.35	75 (67-83)	74 (65-83)	0.43	75 (67-83)	73 (64-82)	0.02	0
NYHA, n(%)			<0.001			<0.001			<0.001	0
I/II	205 (92)	159 (65)		262 (87)	102 (62)		283 (86)	81 (58)		
III/IV	18 (8)	85 (35)		40 (13)	63 (38)		44 (14)	59 (42)		
HF phenotype, n(%)			0.007			0.10			0.09	0
HeFREF	153 (69)	138 (57)		201 (67)	90 (54)		212 (65)	79 (56)		
HeFNEF	70 (31)	106 (43)		101 (33)	75 (46)		115 (35)	61 (44)		
LVEF (%)	45 (35-54)	45 (35-55)	0.86	45 (34-54)	45 (35-56)	0.26	45 (35-54)	45 (35-55)	0.87	160

LV impairment, n(%) None-mild Moderate-severe	 113 (51) 110 (49)	 139 (57) 105 (43)	0.17	 154 (51) 148 (49)	 98 (59) 67 (41)	0.08	 168 (51) 159 (49)	 84 (60) 56 (40)	0.09	0
Height (m)	1.70 (1.64-1.76)	1.66 (1.59-1.74)	<0.001	1.70 (1.63-1.75)	1.65 (1.59-1.74)	0.001	1.69 (1.62-1.75)	1.65 (1.59-1.74)	0.003	0
Weight (kg)	86 (74-102)	79 (66-96)	0.006	84 (72-99)	78 (66-97)	0.05	84 (72-99)	78 (64-97)	0.003	0
BMI (kg/m^2)	29.4 (26.0-33.3)	28.7 (24.4-32.8)	0.15	29.1 (25.6-33.2)	28.8 (24.3-33.1)	0.52	29.1 (25.8-33.3)	28.6 (23.6-32.7)	0.07	0
BMI categories (kg/m^2) <24.9 25.0-29.9 ≥30.0	 44 (20) 79 (35) 100 (45)	 67 (28) 79 (32) 98 (40)	0.15	 65 (22) 110 (36) 127 (42)	 46 (28) 48 (29) 71 (43)	0.17	 65 (20) 119 (36) 143 (44)	 46 (33) 39 (28) 55 (39)	0.009	0
Comorbidities										
Charlson score	7 (5-9)	9 (8-11)	<0.001	7 (5-9)	10 (9-12)	<0.001	8 (6-9)	10 (8-12)	<0.001	0
MI, n(%)	98 (44)	100 (41)	0.52	121 (40)	77 (47)	0.17	142 (43)	56 (40)	0.49	0
PVD, n(%)	28 (13)	44 (18)	0.10	34 (11)	38 (23)	0.001	42 (13)	30 (21)	0.02	0
HTN, n(%)	139 (62)	174 (71)	0.04	192 (64)	121 (73)	0.03	221 (68)	92 (66)	0.69	0
CVA/TIA, n(%)	22 (10)	49 (20)	0.002	26 (9)	45 (27)	<0.001	37 (11)	34 (24)	<0.001	0
Diabetes, n (%)	69 (31)	94 (39)	0.05	90 (30)	73 (44)	0.002	106 (33)	57 (41)	0.21	0
Dementia, n(%)	4 (2)	44 (18)	<0.001	8 (3)	40 (24)	<0.001	5 (2)	43 (31)	<0.001	0
COPD, n(%)	47 (21)	93 (38)	<0.001	73 (24)	67 (41)	<0.001	78 (24)	62 (44)	<0.001	0

Depression, n(%)	28 (13)	65 (27)	<0.001	42 (14)	51 (31)	<0.001	48 (15)	45 (32)	<0.001	0
Anaemia, n(%)	77 (35)	141 (58)	<0.001	110 (36)	108 (66)	<0.001	126 (39)	92 (66)	<0.001	0
Recurrent falls, n(%)	32 (14)	141 (58)	<0.001	63 (21)	110 (67)	<0.001	83 (25)	90 (64)	<0.001	0
Incontinence, n(%)	8 (4)	25 (10)	0.005	11 (4)	22 (13)	0.001	13 (4)	20 (14)	<0.001	0
Medications										
BB, n(%)	201 (90)	191 (78)	<0.001	263 (87)	129 (78)	0.01	280 (86)	112 (80)	0.13	0
ACEi/ARB, n(%)	202 (91)	187 (77)	<0.001	274 (91)	115 (70)	<0.001	291 (89)	98 (70)	<0.001	0
MRA, n(%)	109 (49)	105 (43)	0.21	153 (51)	61 (37)	0.005	162 (50)	52 (37)	0.01	0
Digoxin, n(%)	42 (19)	58 (24)	0.19	69 (23)	31 (19)	0.31	69 (21)	31 (22)	0.80	0
Loop diuretic, n(%)	146 (66)	201 (82)	<0.001	213 (71)	134 (81)	0.01	230 (70)	117 (84)	0.003	0
Thiazide, n(%)	4 (2)	13 (5)	0.04	5 (2)	12 (7)	0.002	9 (3)	8 (6)	0.12	0
≥5 medications, n (%)	176 (79)	228 (93)	<0.001	247 (82)	157 (95)	<0.001	269 (82)	135 (96)	<0.001	0
Blood tests										
NTproBNP (ng/L)	1020 (436-2124)	2465 (1372-4143)	<0.001	919 (402-1899)	1669 (812-3426)	<0.001	963 (426-1919)	2613 (1013-4712)	<0.001	2
Hb (g/dL)	132 (120-143)	121 (110-131)	<0.001	135 (123-144)	121 (112-134)	<0.001	134 (121-144)	120 (109-131)	<0.001	0
Na (mmol/L)	137 (135-138)	136 (133-138)	0.05	137 (135-138)	136 (134-138)	0.09	137 (135-138)	136 (134-138)	0.22	0
K (mmol/L)	4.4 (4.2-4.7)	4.3 (4.1-4.8)	0.32	4.5 (4.2-4.7)	4.4 (4.1-4.7)	0.11	4.5 (4.2-4.7)	4.3 (4.1-4.6)	0.007	0
eGFR (mL/min per 1.73 m^2)	59	55	0.99	61	48	0.004	56	52	0.02	0

	(37-76)	(40-73)		(45-76)	(32-63)		(41-74)	(33-70)		
Frailty screening/ assessments										
Frailty screening										0
CFS (>4), n(%)	14 (6)	192 (79)	<0.001	52 (17)	154 (93)	<0.001	72 (22)	134 (96)	<0.001	
AFN (frail), n(%)	45 (20)	172 (70)	<0.001	88 (29)	129 (78)	<0.001	102 (31)	115 (82)	<0.001	
DFI (frail), n(%)	51 (23)	173 (71)	<0.001	105 (35)	119 (72)	<0.001	118 (36)	106 (76)	<0.001	

HF= heart failure, HR= heart rate, BP= blood pressure, NYHA= new York heart association, HeFREF= heart failure with reduced ejection fraction, HeFNEF= heart failure with normal ejection fraction, LVEF= left ventricular ejection fraction, BMI= body mass index, MI= myocardial infarction, PVD= peripheral vascular disease, HTN= hypertension, CVA/TIA= cerebrovascular accident/ transient ischaemic attack, COPD= chronic obstructive pulmonary disease, BB= beta-blocker, ACEi= angiotensin converting enzyme inhibitor, ARB= angiotensin receptor blocker, MRA= mineralocorticoid receptor antagonist, NTproBNP= N-terminal pro-B-type natriuretic peptide, Hb= haemoglobin, Na= sodium, K= potassium, eGFR = estimated glomerular filtration rate, 5m= 5 meter, TUGT= timed get up and go test, CFS= clinical frailty scale, AFN= acute frailty network frailty criteria, DFI= Derby frailty index.

Table 2. Prevalence of pre-frailty and frailty in HF vs controls according to different frailty tools.

	PRE-FRAILTY				FRAILTY						
					Assessment tools				Screening tools		
	Fried 1-2 (N=184)	**DI** middle tertile (N=177)		**EFS** 6-7 (N=93)	**Fried** ≥3 (N=250)	**DI** upper tertile (N=193)		**EFS** ≥8 (N=142)	**CFS** >4 (N=209)	**AFN** Frail (N=230)	**DFI** Frail (N=230)
		DI<0.15	DI<0.25			DI=0.40-0.49	DI≥0.5				
HF (N=467)	32% (N=148)	0	22% (N=32)	19% (N=90)	52% (N=244)	35% (N=57)	29% (N=48)	30% (N=140)	44% (N=206)	47% (N=217)	48% (N=224)
Controls (N=87)	41% (N=36)	70% (N=21)	100% (N=30)	3% (N=3)	7% (N=6)	7% (N=2)	4% (N=1)	2% (N=2)	3% (N=3)	15% (N=13)	7% (N=6)
P (HF vs controls)	0.08	NA		<0.001	<0.001	NA		<0.001	<0.001	<0.001	<0.001

HF= heart failure, Fried= fried criteria, DI= deficit index, EFS= Edmonton frailty scale, CFS= clinical frailty scale, AFN= acute frailty network frailty criteria, DFI= derby frailty index.

Table 3. Prevalence of frailty in different subgroups of patients with CHF.

		FRAILTY					
		Assessment tools			Screening tools		
		Fried (N=250)	**DI** (N=165)	**EFS** (N=142)	**CFS** (N=209)	**AFN** (N=230)	**DFI** (N=230)
Heart rhythm	**SR** (N=252)	46% (N=116)	32% (N=80)	25% (N=64)	39% (N=98)	40% (N=100)	43% (N=108)
	AF (N=215)	60% (N=128)	40% (N=85)	35% (N=76)	50% (N=108)	54% (N=117)	54% (N=116)
	P (SR vs AF)	0.004	0.02	0.02	0.02	0.001	0.02
BMI categories (kg/m^2)	**<24.9** (N=111)	60% (N=67)	41% (N=46)	41% (N=46)	53% (N=59)	62% (N=69)	64% (N=71)
	25.0-29.9 (N=158)	50% (N=79)	30% (N=48)	25% (N=39)	42% (N=66)	45% (N=71)	54% (N=86)
	≥30 (N=198)	50% (N=98)	36% (N=71)	28% (N=55)	41% (N=81)	39% (N=77)	34% (N=67)
	P (BMI categories)	0.15	0.17	0.009	0.09	<0.001	<0.001
HF phenotype	**HeFREF** (N=291)	47% (N=138)	31% (N=90)	27% (N=79)	40% (N=117)	39% (N=114)	42% (N=122)
	HeFNEF (N=176)	60% (N=106)	43% (N=75)	35% (N=61)	51% (N=89)	59% (N=103)	58% (N=102)
	P (HeFREF vs HeFNEF)	0.007	0.01	0.09	0.03	<0.001	0.001
NYHA	**I/II** (N=364)	44% (N=159)	28% (N=102)	22% (N=81)	35% (N=128)	40% (N=145)	42% (N=154)
	III/IV (N=103)	83% (N=85)	61% (N=63)	57% (N=59)	76% (N=78)	70% (N=72)	68% (N=70)
	P (I/II vs III/IV)	<0.001					
NTproBNP (ng/L)	**<1000** (N=215)	41% (N=88)	26% (N=56)	22% (N=47)	33% (N=70)	32% (N=68)	35% (N=76)
	1000-2000 (N=108)	55% (N=59)	35% (N=38)	30% (N=32)	45% (N=49)	52% (N=56)	54% (N=58)
	>2000 (N=144)	67% (N=97)	49% (N=71)	42% (N=61)	60% (N=87)	65% (N=93)	63% (N=90)
	P (NTproBNP categories)	<0.001					

Age (years)	**<65** (N=82)	28% (N=23)	20% (N=16)	12% (N=10)	22% (N=18)	NA	NA
	65-75 (N=139)	35% (N=49)	23% (N=32)	18% (N=25)	27% (N=38)	32% (N=44)	9% (N=13)
	>75 (N=246)	70% (N=172)	48% (N=117)	43% (N=105)	61% (N=150)	70% (N=173)	86% (N=211)
	P (Age categories)	<0.001					

Fried= fried criteria, DI= deficit index, EFS= Edmonton frailty scale, CFS= clinical frailty scale, AFN= acute frailty network frailty criteria, DFI= derby frailty index, SR= sinus rhythm, AF= atrial fibrillation, BMI= body mass index, HeFREF= heart failure with reduced ejection fraction, HeFNEF= heart failure with normal ejection fraction, NYHA= New York heart association classification, NTproBNP= N-terminal pro B type natriuretic peptide.

Table 4: Correlation coefficients for frailty tools

Indices		Screening tools			Assessment tools	
		DFI	AFN	CFS	Fried	EFS
Screening tools	AFN	0.60				
	CFS	0.54	0.59			
Assessment tools	Fried	0.54	0.57	0.86		
	EFS	0.50	0.56	0.89	0.81	
	DI	0.48	0.53	0.87	0.77	0.86

AFN= acute frailty network frailty criteria, DFI= derby frailty index, CFS= clinical frailty scale, Fried = Fried criteria, EFS= Edmonton frailty scale, DI= deficit index.

All p values < 0.001.

Table 5. Agreement between frailty screening vs assessment tools

FRAILTY			SCREENING TOOLS					
			CFS		AFN		DFI	
			Non-frail (N=261)	Frail (N=206)	Non-frail (N=250)	Frail (N=217)	Non-frail (N=243)	Frail (N=224)
ASSESSMENT TOOLS	FRIED	Non-frail (N=223)	45% (N=209)	3% (N=14)	38% (N=178)	10% (N=45)	37% (N=172)	11% (N=51)
		Frail (N=244)	11% (N=52)	41% (N=192)	15% (N=72)	37% (N=172)	15% (N=71)	37% (N=173)
			K=0.72 P<0.001		K=0.50 P<0.001		K=0.48 P<0.001	
	DI	Non-frail (N=302)	54% (N=250)	11% (N=52)	46% (N=214)	19% (N=88)	42% (N=197)	22% (N=105)
		Frail (N=165)	2% (N=11)	33% (N=154)	8% (N=36)	27% (N=129)	10% (N=46)	26% (N=119)
			K=0.72 P<0.001		K=0.46 P<0.001		K=0.35 P<0.001	
	EFS	Non-frail (N=327)	55% (N=255)	15% (N=72)	48% (N=225)	22% (N=102)	45% (N=209)	25% (N=118)
		Frail (N=140)	1% (N=6)	29% (N=134)	5% (N=25)	25% (N=115)	7% (N=34)	23% (N=106)
			K=0.65 P<0.001		K=0.44 P<0.001		K=0.34 P<0.001	

CFS= clinical frailty scale, AFN= acute frailty network frailty criteria, DFI= derby frailty index, Fried= fried criteria, DI= deficit index, EFS= Edmonton frailty scale, K= kappa coefficient

Table 6. Sensitivity, specificity and misclassification rates of different frailty tools (screening vs assessment vs single physical tests) in identifying frailty according to the combined index

	Frailty tools								
	Screening			**Assessment**			**Single physical tests**		
	CFS >4	**AFN (Frail)**	**DFI (Frail)**	**Fried ≥3**	**EFS ≥8**	**DI (upper tercile)**	**Grip strength***	**5m walk test***	**TUGT >10sec**
Sensitivity (%)	87	79	76	93	62	75	93	95	97
Specificity (%)	89	78	73	76	98	92	58	59	55
PPV (%)	86	72	67	73	96	88	61	62	66
NPV (%)	90	83	81	94	74	81	92	94	96
False positive (%)	6	13	16	14	1	5	25	24	24
False negative (%)	6	9	10	3	18	12	3	2	1
Misclassification rate (%)	12	22	26	17	19	17	28	26	25

(the presumed gold standard for identifying frailty).

EFS= Edmonton frailty scale, DI= deficit index, Fried= Fried criteria, DFI= derby frailty index, AFN= acute frailty network frailty criteria, CFS= clinical frailty scale, 5m= 5 meter, TUGT= timed get up and go test, PPV= positive predictive value, NPV= negative predictive value.

* frail according to Fried criteria